§ 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to our Deposit Account No. 19-0036.

## *Amendments*

***In the Claims:***

Please substitute the following claims 1, 46, 59, 76 and 78 for the pending claims 1, 46, 59, 76 and 78:

1. (Twice amended) A pharmaceutical composition, comprising:

(a) a polypeptide comprising Ser (69) - Ser (208) of SEQ ID NO:2 in a concentration range of about 0.02 to about 40 mg/ml (w/v);

(b) a buffer having a buffering capacity of about pH 5.0 to about pH 8.0 at a concentration range of about 5 mM to about 50 mM;

(c) a pharmaceutically acceptable diluent to bring the composition to a designated volume; and

(d) a preservative selected from the group consisting of m-cresol, chlorobutanol, and a mixture of methyl paraben and propyl paraben.

50. (Once amended) The pharmaceutical composition of claim ~~44~~ 48, wherein said etherified cellulose is methylcellulose, hydroxyethyl cellulose, hydroxy propyl cellulose, hydroxy propyl methylcellulose, or carboxymethyl cellulose.

~~59~~ 54. (Once amended) The composition of claim ~~58~~ 55, wherein said gel forming agent is (1) a vinyl polymer selected from the group consisting of polyacrylic acid, polymethacrylic acid, polyvinyl pyrrolidone polyvinyl alcohol, and salts and esters thereof; or (2) a polysaccharide selected from the group consisting of a cellulose derivative, a glycosaminoglycan, agar, pectin, alginic acid, dextran, α-amylose, amylopectin, chitosan, and salts or esters thereof.

B3

~~76~~ 70. (Twice amended) A pharmaceutical composition comprising:

(a) about 3.3 mg/ml of a polypeptide comprising Ser (69) - Ser (208) of SEQ ID NO:2;

(b) 10 mM sodium citrate

(c) 20 mM sodium chloride;

(d) 1 mM EDTA

(e) 2% w/v glycine;

(f) 0.5% w/v sucrose; and

(g) water;

wherein the composition is at a pH of about 6.2.

B4

~~78~~ 73. (Twice amended) A pharmaceutical composition comprising:

(a) about 1.0 mg/ml of a polypeptide comprising Ser (69) - Ser (208) of SEQ ID NO:2;

(b) 10 mM sodium citrate;

(b) 0.46% hydroxyethylcellulose;

B5

(c) 7% sucrose;

(d) 20 mM sodium citrate;

(e) 20 mM sodium chloride; and

(f) 1 mM EDTA;

wherein the composition is at a pH of about 6.2.

Please add the following new claims:

~~82~~ 75. (New) A pharmaceutical composition produced by the process of admixing:

(a) a polypeptide comprising Ser (69) - Ser (208) of SEQ ID NO:2 in a concentration range of about 0.02 to about 40 mg/ml (w/v);

(b) a buffer having a buffering capacity of about pH 5.0 to about pH 8.0 at a concentration range of about 5 mM to about 50 mM;

(c) a pharmaceutically acceptable diluent to bring the composition to a designated volume; and

(d) a preservative selected from the group consisting of m-cresol, chlorobutanol, and a mixture of methyl paraben and propyl paraben.

~~83~~ 76. (New) The pharmaceutical composition of claim ~~82~~ 75, further comprising one or more of:

(a) a chelating agent at a concentration range of about 0 mM to about 10 mM; and

(b) a tonicifier at a concentration range of about 0 mM to about 150 mM.

84. (New) The pharmaceutical composition of claim 83, wherein said tonicifier is selected from the group consisting of NaCl, glycine, sucrose, mannitol, and mixtures thereof.

85. (New) The pharmaceutical composition of claim 82, further comprising one of:

(a) about 0.5% to about 2% w/v glycerol,

(b) about 0.1% to about 1% w/v methionine, or

(c) about 0.1% to about 2% w/v monothioglycerol.

86. (New) The pharmaceutical composition of claim 82, wherein said polypeptide is present in a concentration range of about 0.05 to about 30 mg/ml (w/v).

87. (New) The pharmaceutical composition of claim 86, wherein said polypeptide is present in a concentration range of about 0.1 to about 20 mg/ml (w/v).

88. (New) The pharmaceutical composition of claim 87, wherein said polypeptide is present in a concentration range of about 0.2 to 4 mg/ml (w/v).

89. (New) The pharmaceutical composition of claim 82, wherein said diluent is water.

90. (New) The pharmaceutical composition of claim 83, wherein said chelating agent is EDTA at a concentration of about 1 mM, and said tonicifier is present at a concentration of about 125 mM.

91. (New) The pharmaceutical composition of claim 82, wherein said pH is from about pH 5.5 to about pH 6.5.

92. (New) The pharmaceutical composition of claim 91, wherein said pH is about pH 6.0.

93. (New) The pharmaceutical composition of claim 82, wherein said buffer is selected from the group consisting of phosphonic, acetic, aconitic, citric, glutaric, malic, succinic carbonic acid, and an alkali or alkaline earth salt thereof.

94. (New) The pharmaceutical composition of claim 93, wherein said buffer is a phosphate, acetate or citrate salt.

95. (New) The pharmaceutical composition of claim 93, wherein said buffer is a citrate salt.

96. (New) The pharmaceutical composition of claim 82, wherein said buffer is present in a concentration range of about 5 mM to about 30 mM.

~~97~~ 91. (New) The pharmaceutical composition of claim ~~96~~ 90, wherein said buffer is a citrate salt present in a concentration of from about 10 mM to about 20 mM.

~~98~~ 92. (New) The pharmaceutical composition of claim ~~82~~ 75, further comprising a stabilizing amount of one or more of (a) an antioxidant or (b) a thiol-compound.

~~99~~ 93. (New) The pharmaceutical composition of claim ~~82~~ 75, wherein said composition is maintained at a temperature at or below -20°C.

~~100~~ 94. (New) The pharmaceutical composition of claim ~~82~~ 75, wherein said polypeptide is selected from the group consisting of: (i) Ser (69) - Ser (208) of SEQ ID NO:2; (ii) Ser (69) - Ser (208) of SEQ ID NO:2 with a methionine at the N-terminus; and (iii) a mixture of (i) and (ii).

~~101~~ 95. (New) The pharmaceutical composition of claim ~~82~~ 75, further comprising a bulking agent.

~~102~~ 109. (New) The pharmaceutical composition of claim ~~101~~ 95, wherein said bulking agent is selected from the group consisting of sucrose, glycine, mannitol, trehalose, and mixtures thereof.

~~103~~ 112. (New) The pharmaceutical composition of claim ~~102~~ 109, wherein said bulking agent is sucrose or a mixture of sucrose and glycine.

104. (New) The pharmaceutical composition of claim 83, further comprising a bulking agent.

105. (New) The pharmaceutical composition of claim 102, wherein said bulking agent is present in a concentration of about 2% to about 10% w/v.

106. (New) The pharmaceutical composition of claim 102, wherein said bulking agent is 5% mannitol, 7% sucrose, 8% trehalose, or 2% glycine + 0.5% sucrose.

107. (New) The pharmaceutical composition of claim 101, wherein said pH is about pH 6.2.

108. (New) The pharmaceutical composition of claim 101, wherein said diluent is water.

109. (New) The pharmaceutical composition of claim 101, wherein said buffer is selected from the group consisting of phosphonic, acetic, aconitic, citric, glutaric, malic, succinic carbonic acid, and an alkali or alkaline earth salt thereof.

110. (New) The pharmaceutical composition of claim 109, wherein said buffer is a phosphate or citrate salt.

111. (New) The pharmaceutical composition of claim 110, wherein said buffer is a citrate salt.

112. (New) The pharmaceutical composition of claim 108, wherein over 90% of the water is removed by lyophilization.

113. (New) The pharmaceutical composition of claim 112, which is reconstituted in with an amount of sterile water effective to maintain isotonic conditions of about 290 mOsm.

114. (New) The pharmaceutical composition of claim 101, wherein said buffer is added in a concentration from about 5 mM to about 50 mM.

115. (New) The pharmaceutical composition of claim 114, wherein said buffer is citrate at a concentration of about 10 mM.

116. (New) The pharmaceutical composition of claim 101, further including a stabilizing amount of one or more of (g) an antioxidant, or (h) a thiol-compound.

117. (New) The pharmaceutical composition of claim 112, wherein said composition is reconstituted in sterile water containing a stabilizing amount of an antioxidant comprising: a) about 0.01% to about 2% w/v monothioglycerol, b) about 0.01%

to about 2% w/v ascorbic acid, c) about 0.01% to about 2% w/v methionine or d) combinations thereof.

113 75
~~118~~. (New) The pharmaceutical composition of claim ~~82~~, further comprising a thickening agent in an amount effective to raise the viscosity to about 50 to about 10,000 cps.

114 113
~~119~~. (New) The pharmaceutical composition of claim ~~118~~, wherein said thickening agent is present in an amount effective to raise the viscosity to about 50 to about 1,000 cps.

115 114
~~120~~. (New) The pharmaceutical composition of claim ~~119~~, wherein said thickening agent in an amount effective to raise the viscosity to about 200 to about 300 cps.

121. (New) The pharmaceutical composition of claim ~~118~~ 75, wherein said thickening agent is present in a concentration of 0 to 5% (w/w).

122. (New) The pharmaceutical composition of claim ~~118~~ 75, wherein said thickening agent is a water soluble etherified cellulose or a carbomer.

124
~~123~~. (New) The pharmaceutical composition of claim 122, wherein said etherified cellulose is an alkyl cellulose, hydroxyalkyl cellulose, carboxyalkyl cellulose or alkylhydroxyalkyl cellulose.

123
~~124~~. (New) The pharmaceutical composition of claim 122, wherein said etherified cellulose is methylcellulose, hydroxyethyl cellulose, hydroxy propyl cellulose, hydroxy propyl methylcellulose, or carboxymethyl cellulose.

124
~~125~~. (New) The pharmaceutical composition of claim 123, ~~124~~, wherein said etherified cellulose derivative has a molecular weight of about 50,000 to about 700,000 and is present in a concentration of about 0 to about 20% by weight.

125
~~126~~. (New) The pharmaceutical composition of claim 124, ~~125~~, wherein said etherified cellulose derivative has a molecular weight of about 80,000 to about 240,000 and is present in a concentration of about 2% to about 8% by weight.

116
~~127~~. (New) The pharmaceutical composition of claim 115, ~~120~~, wherein said buffer is citrate in a concentration of about 10 mM to about 50 mM.

117
~~128~~. (New) The pharmaceutical composition of claim 116, ~~127~~, wherein said buffer is citrate in a concentration of about 10 mM to about 20 mM citrate.

118
~~129~~. (New) The pharmaceutical composition of claim 116, ~~127~~, wherein said bulking agent is sucrose in a concentration of about 0.01% to about 5% sucrose.

119
~~130~~. (New) The pharmaceutical composition of claim 118, ~~129~~, wherein said thickening agent is added directly to a liquid formulation and thereafter lyophilized.

131. (New) The pharmaceutical composition of claim 129, wherein said thickening agent is added to a lyophilized formulation by reconstituting said formulation by adding a suitable diluent having a thickening agent dissolved therein.

132. (New) The pharmaceutical composition of claim 101, further comprising a thickening agent in an amount effective to raise the viscosity to about 50 to about 10,000 cps.

133. (New) The composition of claim 82, further comprising a gelling agent in an amount effective to raise the viscosity to about 0.1 to about 10,000 cps at room temperature.

134. (New) The composition of claim 101, further comprising a gelling agent in an amount effective to raise the viscosity to about 0.1 to about 10,000 cps at room temperature.

135. (New) The composition of claim 133, wherein said gel forming agent is a water-soluble polymer capable of forming a viscous aqueous solution, or non-water soluble, water-swellable polymer capable of forming a viscous solution.

136. (New) The composition of claim 135, wherein said gel forming agent is a high molecular weight polymer selected from the group consisting of vinyl polymer,

polyoxyethylene-polyoxypropylene copolymer, polysaccharide, protein, poly(ethylene oxide), acrylamide polymer or a salt thereof.

130 ~~137~~. (New) The composition of claim 129 ~~136~~, wherein said gel forming agent is (1) a vinyl polymer selected from the group consisting of polyacrylic acid, polymethacrylic acid, polyvinyl pyrrolidone polyvinyl alcohol, and salts and esters thereof; or (2) a polysaccharide selected from the group consisting of a cellulose derivative, a glycosaminoglycan, agar, pectin, alginic acid, dextran, α-amylose, amylopectin, chitosan, and salts or esters thereof.

131 ~~138~~. (New) The composition of claim 129 ~~136~~, wherein said gel forming agent is a glycosaminoglycan selected from the group consisting of hyaluronic acid, chondroitin, chondroitin-4-sulfate, heparan sulfate, heparin and salts and esters thereof.

132 ~~139~~. (New) The composition of claim 131 ~~138~~, wherein said glycosaminoglycan is present in combination with collagen, gelatin, or fibronectin.

133 ~~140~~. (New) The composition of claim 129 ~~136~~, wherein said gel forming agent is an acrylamide polymer selected from the group consisting of a polyacrylamide or a polymethacrylamide.

134 ~~141~~. (New) The composition of claim 128 ~~136~~, wherein said gel forming agent is a polyoxyethylene-polyoxypropylene block copolymer.

135 142. (New) The composition of claim 134 141, which comprises about 10 to about 60% by weight of a polyoxyethylene-polyoxypropylene block copolymer having an average molecular weight of about 500 to 50,000.

136 143. (New) The composition of claim 135 142, which comprises about 14 to about 18% by weight of a polyoxyethylene-polyoxypropylene block copolymer having a molecular weight in the range 1,000 to 15,000.

137 144. (New) The pharmaceutical composition of claim 75 82, wherein said polypeptide is present in a concentration range of about 0.01 mg/ml to about 10 mg/ml (w/v).

138 145. (New) The pharmaceutical composition of claim 75 82, further comprising one of:

(a) lysine;

(b) hydroxypropyl-β-cyclodextrin; and

(c) sulfated-β-cyclodextrin;

or combinations thereof.

139 146. (New) The pharmaceutical composition of claim 75 82, wherein said preservative is a mixture of methyl paraben and propyl paraben.

146 ~~147~~. (New) The pharmaceutical composition of claim 139 ~~146~~, wherein said composition comprises 0.18% methyl paraben and 0.02% propyl paraben.

141 ~~148~~. (New) A pharmaceutical composition produced by the process of admixing:

(a) about 1.0 mg/ml of a polypeptide comprising Ser (69) - Ser (208) of SEQ ID NO:2;

(b) 20mM citrate, pH 5-5.5; and

(c) 0.01% polysorbate 80.

Be

142 ~~149~~. (New) The pharmaceutical composition of claim 141 ~~148~~, further comprising 1 mM EDTA.

dep

143 ~~150~~. (New) The pharmaceutical composition of claim 141 ~~148~~, wherein said polypeptide is selected from the group consisting of: (i) Ser (69) - Ser (208) of SEQ ID NO:2; (ii) Ser (69) - Ser (208) of SEQ ID NO:2 with a methionine at the N-terminus; and (iii) a mixture of (i) and (ii).

144 ~~151~~. (New) A pharmaceutical composition produced by the process of admixing:

(a) about 3.3 mg/ml of a polypeptide comprising Ser (69) - Ser (208) of SEQ ID NO:2;

(b) 10 mM sodium citrate

(c) 20 mM sodium chloride;

(d) 1 mM EDTA

(e) 2% w/v glycine;

(f) 0.5% w/v sucrose; and

(g) water;

wherein the composition is at a pH of about 6.2.

145 ~~152.~~ (New) The pharmaceutical composition of claim 144 ~~151~~, wherein over 90% of the water is removed by lyophilization.

B4

146 ~~153.~~ (New) The pharmaceutical composition of claim 144 ~~151~~, wherein said polypeptide is selected from the group consisting of: (i) Ser (69) - Ser (208) of SEQ ID NO:2; (ii) Ser (69) - Ser (208) of SEQ ID NO:2 with a methionine at the N-terminus; and (iii) a mixture of (i) and (ii).

147 ~~154.~~ (New) A pharmaceutical composition produced by the process of admixing:

(a) about 1.0 mg/ml of a polypeptide comprising Ser (69) - Ser (208) of SEQ ID NO:2;

(b) 10 mM sodium citrate;

(b) 0.46% hydroxyethylcellulose;

(c) 7% sucrose;

(d) 20 mM sodium citrate;

(e) 20 mM sodium chloride; and

(f) 1 mM EDTA;

wherein the composition is at a pH of about 6.2.

148
~~155~~. (New) The pharmaceutical composition of claim 147, ~~154~~, wherein said polypeptide is selected from the group consisting of: (i) Ser (69) - Ser (208) of SEQ ID NO:2; (ii) Ser (69) - Ser (208) of SEQ ID NO:2 with a methionine at the N-terminus; and (iii) a mixture of (i) and (ii).